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(54) Title: PHENYLALANINE DERIVATIVES AS DIPEPTIDYL PEPTIDASE INHIBITORS FOR THE TREATMENT OR PREVENTION OF DIABETES

(57) Abstract: The present invention is directed to phenylalanine derivatives which are inhibitors of the dipeptidyl peptidase-IV enzyme ("DP-IV inhibitors") and which are useful in the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as diabetes and particularly type 2 diabetes. The invention is also directed to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which the dipeptidyl peptidase-IV enzyme is involved.

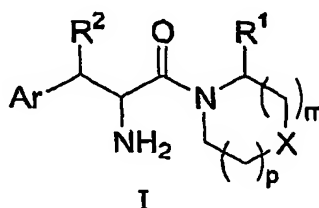


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AMENDED CLAIMS

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1. A compound of structural formula I:



- 5 or a pharmaceutically acceptable salt thereof; wherein
each n is independently 0, 1, or 2;
m and p are independently 0 or 1;
q is 1 or 2;

- 10 X is CH₂, S, CHF, or CF₂;

Ar is phenyl, unsubstituted or substituted with one to five R³ substituents;

R¹ is hydrogen;

15

R² is selected from the group consisting of

C₁₋₁₀ alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents
independently selected from halogen or hydroxy,

C₂₋₁₀ alkenyl, wherein alkenyl is unsubstituted or substituted with one to five

20

substituents independently selected from halogen or hydroxy,

(CH₂)_n-aryl, wherein aryl is unsubstituted or substituted with one to five substituents
independently selected hydroxy, halogen, CO₂H, C₁₋₆ alkyloxycarbonyl, C₁₋₆
alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted
with one to five halogens,

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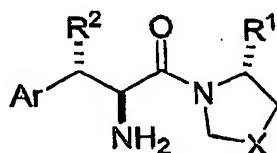
(CH₂)_n-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three
substituents independently selected from hydroxy, halogen, CO₂H, C₁₋₆
alkyloxycarbonyl, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are
unsubstituted or substituted with one to five halogens,

[(tetrazol-5-yl)amino]carbonyl.

15. The compound of Claim 14 wherein R³ is selected from the group consisting of:

5 fluoro,
chloro,
bromo,
trifluoromethyl,
trifluoromethoxy, and
10 methoxy.

16. The compound of Claim 1 of the structural formula Ij



(Ij)

wherein X is CH₂, S, CHF, or CF₂;

15 Ar is phenyl, unsubstituted or substituted with one to five R³ substituents;
R¹ is hydrogen;

R² is selected from the group consisting of

C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents

20 independently selected from halogen or hydroxy,

(CH₂)_n-C₃₋₆ cycloalkyl,

COOH,

COOC₁₋₆ alkyl, and

25 CONR⁴R⁵, wherein R⁴ and R⁵ are independently selected from the group consisting of
hydrogen, tetrazolyl, thiazolyl, (CH₂)_n-phenyl, (CH₂)_n-C₃₋₆ cycloalkyl, and C₁₋₆
alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and
wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five
substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆

alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

or R⁴ and R⁵ together with the nitrogen atom to which they are attached form a heterocyclic ring selected from pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and

each R³ is independently selected from the group consisting of:

halogen,

C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five

halogens,

C₁₋₆ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five

halogens,

phenyloxy, unsubstituted or substituted with one to three substituents

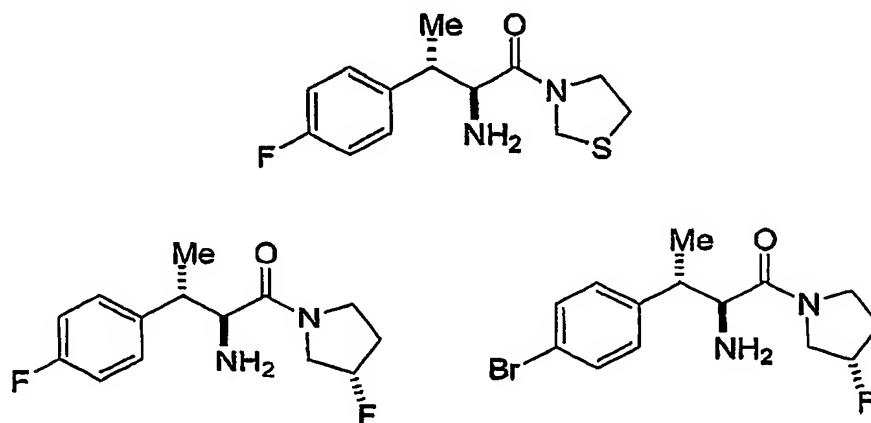
independently selected from halogen and cyano, and

phenyl(CH₂)_nCON(Me)-, wherein phenyl is unsubstituted or

substituted with one to three substituents independently

selected from halogen, trifluoromethyl, and C₁₋₄ alkyl.

17. The compound of Claim 16 of the structural formula selected from the group consisting of



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Statement under Article 19(1)

Claims 1, 16 and 17 of the international application have been amended to exclude compounds disclosed in WO 03/002530 cited in the International Search Report . The present amendment does not introduce new matter and is fully supported by Applicants' description. The present amendment has no impact on the description and the drawings of the international application.